K011505

JUL - 2 2001

510(k) Summary of Safety and Effectiveness

This summary of safety and effectiveness information has been prepared in accordance with the requirements of SMDA 1990 and 21 CFR Part 807.92.

Name: **Address:**	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045-5597
Telephone Number: **Facsimile Number:**	(310) 645-8200 (310) 645-9999
Contact Person:	Edward M. Levine, Ph.D. Director, Clinical Affairs
Date of Preparation:	May 15, 2001
Device Name:	
Trade:	IMMULITE® Intact PTH IMMULITE® 2000 Intact PTH
Catalog Number:	LKPP1 (100 tests), LKPP5 (500 tests) L2KPP2 (200 tests), L2KPP6 (600 tests)
CFR:	A parathyroid hormone test system is a device intended to measure the levels of parathyroid hormone in serum and plasma. Measurements of parathyroid hormone levels are used in the differential diagnosis of hypercalcemia (abnormally high levels of calcium in the blood) and hypocalcemia (abnormally low levels of calcium in the blood) resulting from disorders of calcium metabolism.
Common:	Reagent system for the determination of parathyroid hormone in plasma.
Classification:	Class II device, 75-CEW (21CFR 862.1545)
Panel:	Clinical Chemistry
CLIA Complexity Category:	We believe the category to be moderate, based on previous classification of analogous tests.
Manufacturer:	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045-5597

Establishment Registration Number: DPC's Registration Number is 2017183

Substantially Equivalent Predicate Device: Nichols Chemiluminescent Intact PTH (K954418)
Nichols IRMA Intact PTH (K771783)

Description of Device: IMMULITE® Intact PTH and IMMULITE® 2000 Intact PTH are solid phase, chemiluminescent enzyme immunometric assays for use with their respective IMMULITE® and IMMULITE® 2000 Automated Analyzers.

Intended Use of the Device:

IMMULITE® Intact PTH and IMMULITE® 2000 Intact PTH are solid-phase, two-site chemiluminescent enzyme immunometric assays for use with their respective IMMULITE® and IMMULITE® 2000 Automated Analyzers and are designed for the quantitative measurement of intact parathyroid hormone (parathyrin, PTH) in EDTA plasma. It is intended strictly for *in vitro* diagnostic use as an aid in the differential diagnosis of hypercalcemia and hypocalcemia.

Technology:

IMMULITE® Intact PTH is a solid-phase, two-site chemiluminescent immunometric assay. The solid phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with an affinity-purified murine monoclonal anti-PTH (44-84) anitbody.

The patient sample and alkaline phosphatase-conjugated affinity purified goat polyclonal anti-PTH (1-34) antibody are incubated for approximately 60 minutes at 37°C in the Test Unit with intermittent agitation, intact PTH in the sample is bound to form an antibody sandwich complex. Unbound conjugate is then removed by a centrifugal wash, after which substrate is added and the Test Unit is incubated for a further 10 minutes.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is proportional to the concentration of intact PTH in the sample.

IMMULITE 2000 Intact PTH is a solid-phase, two-site chemiluminescent immunometric assay. The solid phase is a polystyrene bead coated with an affinity-purified murine monoclonal anti-PTH (44-84) anitbody.

The patient sample and alkaline phosphatase-conjugated affinity-purified goat polyclonal anti-PTH (1-34) antibody are introduced into the Reaction Tube containing the bead and incubated for approximately 60 minutes at 37°C with intermittent agitation. During this time, intact PTH in the sample is bound to form an antibody sandwich complex. Unbound conjugate is then removed by a centrifugal wash, after which substrate is added and the Reaction Tube is incubated for a further 5 minutes.

Technology (continued):

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is proportional to the concentration of intact PTH in the sample.

Nichols Chemiluminescent Intact PTH is a chemiluminescent immunometric assay utilizing a goat polyclonal antibody to PTH immobilized on a polystyrene bead and another goat polyclonal antibody to PTH labeled with an acridinium ester. The serum sample is added to a tube followed by the addition of the chemiluminescent labeled antibody reagent. An antibody coated bead is then added to the reactants. The polyclonal antibody on the bead together with the labeled polyclonal antibody bind the PTH in the sample to form a sandwich-complex. Free labeled antibody is separated from the labeled antibody bound to the bead by aspiration of the reaction mixture and subsequent washing. The tubes containing the washed beads are placed into the luminometer, which automatically injects Trigger Solutions 1 and 2, initiating the chemiluminescent reaction. The light is quantitated by the luminometer and expressed in relative light units (RLU). The amount of bound labeled antibody is directly proportional to the concentration of PTH in the sample. A standard curve is generated by plotting the RLU versus the respective PTH concentration for each standard on logarithmic scales. The concentration of PTH in the unknown sample is determined directly from the standard curve.

Nichols Institute Diagnostics utilizes chemiluminescence acridinium esters as the label in its chemiluminescence immunoassay kits. Acridium esters emit light upon treatment with hydrogen peroxide and an alkaline solution. The Trigger 1 solution contains hydrogen peroxide in dilute acid and Trigger 2 solution contains dilute sodium hydroxide. The luminometer automatically injects Trigger solutions 1 and 2 into the assay tubes which oxidize the acridinium ester. The oxidized product is in an excited state. The subsequent return to ground state results in emission of light which is quantified in 2 seconds and is expressed in RLU by the luminometer.

Nichols IRMA Intact PTH is a two-site immunoradiometric assay (IRMA) for the measurement of the biologically intact 84 amino acid chain of PTH. Two different goat polyclonal antibodies to human PTH have been purified by affinity chromatography to be specific for well defined regions on the PTH molecule. One antibody is prepared to bind only the mid-region and C-terminal PTH 38-84 and this antibody is immobilized onto plastic beads. The other antibody is prepared to bind only the N-terminal PTH 1-34 and this antibody is radiolabeled for detection.

The sample containing PTH is incubated simultaneously with an antibody-coated bead and 125I-labeled antibody. Intact PTH present in the sample is bound by both the immobilized and labeled antibodies to form a "sandwich" complex:

$$\text{Bead Anti-PTH (39-84)} - \text{Intact PTH (1-84)} - {}^{125}\text{I Anti-PTH (1-34)}$$

Although mid-region and C-terminal fragments are bound by the antibody coated bead, only the intact PTH 1-84 forms the sandwich complex necessary for detection. The capacity of the immobilized antibody has been adjusted to exhibit no interference by inactive fragments, even at very elevated levels.

Technology (continued):

At the end of the assay incubation, the bead is washed to remove unbound components and the radioactivity bound to the solid phase is measured in a gamma counter. Since the formation of a sandwich complex occurs only in the presence of an intact PTH molecule, the radioactivity of the bead bound complex is directly proportional to the amount of intact PTH in the sample.

A dose response curve of radioactivity vs. concentration is generated using results obtained from standards which are assayed concurrently with the unknows. Concentrations of intact PTH present in the controls and patient samples are determined directly from this curve.

Performance Equivalence:

Diagnostic Products Corporation asserts that IMMULITE® Intact PTH and IMMULITE® 2000 Intact PTH produce substantially equivalent results to other commercially marketed intact PTH assays, such as Nichols Chemiluminescent Intact PTH and Nichols IRMA Intact PTH. The Nichols Chemiluminescent Intact PTH assay utilizes chemiluminescence acridinium esters technology. The Nichols IRMA Intact PTH assay utilizes radioactive technology. Each product is designed for the quantitative measurement of intact parathyroid hormone (parathryrin, PTH) in EDTA plasma as an aid in the differential diagnosis of hypercalcemia and hypocalcemia.

Method Comparison:

The IMMULITE® Intact PTH procedure was compared to a commercially available assay, Nichols Chemiluminescent Intact PTH, on 85 EDTA plasma samples, with PTH concentrations ranging from 5 to approximately 500 pg/mL. Linear regression analysis yielded the following statistics:

(IMMULITE) = 1.01 (Nichols Chemiluminescent) – 5.9 pg/mL r = 0.967

Means: 142 pg/mL (IMMULITE)
148 pg/mL (Nichols Chemiluminescent)

In a second comparison, the IMMULITE® Intact PTH procedure was compared to a commercially available assay, Nichols IRMA Intact PTH, on 196 EDTA plasma samples, with PTH concentrations ranging from 5 to approximately 500 pg/mL. Linear regression analysis yielded the following statistics:

(IMMULITE) = 0.91 (Nichols IRMA) + 1.3 pg/mL r = 0.976

Means: 104 pg/mL (IMMULITE)
113 pg/mL (Nichols IRMA)

Method Comparison (continued):

The IMMULITE® 2000 Intact PTH procedure was compared to a commercially available assay, Nichols Chemiluminescent Intact PTH, on 85 EDTA plasma samples, with PTH concentrations ranging from 5 to approximately 500 pg/mL. Linear regression analysis yielded the following statistics:

(IMMULITE 2000) = 1.08 (Nichols Chemiluminescent) – 8.0 pg/mL r = 0.963

Means: 151 pg/mL (IMMULITE 2000)
148 pg/mL (Nichols Chemiluminescent)

In a second comparison, the IMMULITE® 2000 Intact PTH procedure was compared to a commercially available assay, Nichols IRMA Intact PTH, on 196 EDTA plasma samples, with PTH concentrations ranging from 5 to approximately 500 pg/mL. Linear regression analysis yielded the following statistics:

(IMMULITE 2000) = 1.00 (Nichols IRMA) – 1.09 pg/mL r = 0.973

Means: 101 pg/mL (IMMULITE 2000)
102 pg/mL (Nichols IRMA)

Conclusion:

The data presented in this summary of safety and effectiveness is the data that the Food and Drug Administration used in granting DPC substantial equivalence for IMMULITE® Intact PTH and IMMULITE® 2000 Intact PTH.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL - 2 2001

Edward M. Levine, Ph.D.
Director, Clinical Affairs
Diagnostics Products Corporation
5700 West 96th Street
Los Angeles, CA 90045-5597

Re: 510(k) Number: K011505
Trade/Device Name: Immulite® Intact PTH and Immulite® 2000 Intact PTH
Regulation Number: 862.1545
Regulatory Class: II
Product Code: CEW
Dated: March 15, 2001
Received: March 16, 2001

Dear Dr. Levine:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K011505
Device Name: IMMULITE® Intact PTH
IMMULITE® 2000 Intact PTH

Indications For Use: The IMMULITE® Intact PTH and IMMULITE® 2000 Intact PTH assays are for *in vitro* diagnostic use with their respective analyzers for the quantitative measurement of intact parathyroid hormone (parathyrin, PTH) in EDTA plasma, as aids in the differential diagnosis of hypercalcemia and hypocalcemia.

Ian Cooper
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K011505

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

✓ Prescription Use (Per 21 CFR 801.109) OR Over-The-Counter Use

(Optional Format 1-2-96)